

# NATIONAL BUREAU OF STANDARDS REPORT

**NBS PROJECT**

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**NBS REPORT**

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ELEVENTH REPORT ON  
A SURVEY OF THERMODYNAMIC PROPERTIES OF THE  
COMPOUNDS OF THE ELEMENTS CHNOPS

George T. Armstrong, George T. Furukawa  
and Martin L. Reilly

Progress Report for the Period 1 January to 31 March 1967

to

National Aeronautics and Space Administration

Contract No. R-138, Amendment 2.

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U.S. DEPARTMENT OF COMMERCE  
NATIONAL BUREAU OF STANDARDS

## FOREWORD

A study at the National Bureau of Standards (NBS), of which this is the eleventh progress report, has been undertaken to meet the need of the National Aeronautics and Space Administration (NASA) for thermodynamic information on biologically related materials important to the space program for several reasons. Among these reasons are the necessity of inferring the maximum account of useful chemistry of incompletely accessible environments, for which only limited information is available, the possibility of the occurrence of organic compounds naturally synthesized under primitive conditions, and the possibility of theoretically recovering part of the prebiological history of the earth.

This program is being carried out under the technical supervision of Dr. George Jacobs of NASA, and with the consultation of Dr. Harold Morowitz of the Yale University, Department of Molecular Biology and Biophysics, and Dr. C. W. Beckett of the Heat Division, Institute for Basic Standards (NBS). The contract (Contract No. R-138) was initiated 1 May 1964 and extended 29 April 1965 and 11 August 1966. The program has been extended by Amendments 1 and 2. This report covers the second quarter of the work being carried out under Amendment 2.

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## Section I.

### Analysis of Heat-Capacity and Vapor Pressure Data

George T. Furukawa and Martin L. Reilly

#### 1. Heat-Capacities

The heat-capacity data on the normal aliphatic saturated hydrocarbons containing 8 to 16 carbons, and on tetraphosphorus decasulfide ( $P_4S_{10}$ ), have been analyzed. The results of the analysis are summarized in the following section in terms of the entropy at 298.15°K ( $S_{298}^0$ ). Literature values of  $S_{298}^0$  are given for comparison. References to the sources of heat-capacity data examined in the analysis are also listed with each substance. The data reported in 1902 by Mabery and Goldstein [1]<sup>1</sup> on the  $C_8$  to  $C_{16}$  hydrocarbons were considered to be only of historical interest and were not given any weight in the analysis. The abbreviation: e.u. (= cal °K<sup>-1</sup> mol<sup>-1</sup>) is used to express the units of entropy.

##### n-octane, $C_8H_{18}$

$S_{298}^0 = 86.30 \pm 0.20$ e.u.	[This work]
= 86.0 e.u.	[2]
= 86.0 e.u.	[3]
= 86.326 $\pm 0.17$ e.u.	[7]

##### Data sources:

(1902), mean 0-50°C	[1]
(1930), 86-294°K	[2]
(1931), 92-298°K	[3]
(1947), 10-35°C	[5]
(1953), 13-298°K	[7]

##### n-nonane, $C_9H_{20}$

$S_{298}^0 = 94.06 \pm 0.30$ e.u.	[This work]
= 93.9 e.u.	[3]
= 94.091 $\pm 0.19$ e.u.	[7]

##### Data sources:

(1902), mean 0-50°C	[1]
(1930), 224-299°K	[2]
(1931), 93-298°K	[3]
(1947), 5-45°C	[5]
(1953), 12-314°K	[7]

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<sup>1</sup> Figures in brackets indicate the literature references at the end of this section.

n-decane, C<sub>10</sub>H<sub>22</sub>

$$\begin{aligned} S_{298}^{\circ} &= 101.77 \pm 0.25 \text{ e.u.} & [\text{This work}] \\ &= 102.5 \text{ e.u.} & [3] \\ &= 101.793 \pm 0.20 \text{ e.u.} & [7] \end{aligned}$$

Data sources:

$$\begin{aligned} (1902), \text{ mean } 0-50^{\circ}\text{C} & [1] \\ (1930), 242-296^{\circ}\text{K} & [2] \\ (1931), 91-298^{\circ}\text{K} & [3] \\ (1947), 5-45^{\circ}\text{K} & [5] \\ (1953), 12-319^{\circ}\text{K} & [7] \end{aligned}$$

n-undecane, C<sub>11</sub>H<sub>24</sub>

$$\begin{aligned} S_{298}^{\circ} &= 109.53 \pm 0.25 \text{ e.u.} & [\text{This work}] \\ &= 110.9 \text{ e.u.} & [3] \\ &= 109.495 \pm 0.22 \text{ e.u.} & [7] \end{aligned}$$

Data sources:

$$\begin{aligned} (1902), \text{ mean } 0-50^{\circ}\text{C} & [1] \\ (1931), 92-298^{\circ}\text{K} & [3] \\ (1953), 12-299^{\circ}\text{K} & [7] \end{aligned}$$

n-dodecane, C<sub>12</sub>H<sub>26</sub>

$$\begin{aligned} S_{298}^{\circ} &= 117.25 \pm 0.30 \text{ e.u.} & [\text{This work}] \\ &= 118.1 \text{ e.u.} & [3] \\ &= 117.267 \pm 0.23 \text{ e.u.} & [7] \end{aligned}$$

Data sources:

$$\begin{aligned} (1902), \text{ mean } 0-50^{\circ}\text{C} & [1] \\ (1931), 93-298^{\circ}\text{K} & [3] \\ (1953), 12-317^{\circ}\text{K} & [7] \end{aligned}$$

n-tridecane, C<sub>13</sub>H<sub>28</sub>

$$\begin{aligned} S_{298}^{\circ} &= 124.96 \pm 0.30 \text{ e.u.} & [\text{This work}] \\ &= 124.966 \pm 0.25 \text{ e.u.} & [7] \end{aligned}$$

Data sources:

$$\begin{aligned} (1902), \text{ mean } 0-50^{\circ}\text{C} & [1] \\ (1953), 12-306^{\circ}\text{K} & [7] \end{aligned}$$

n-tetradecane, C<sub>14</sub>H<sub>30</sub>

$$\begin{aligned} S_{298}^{\circ} &= 132.73 \pm 0.30 \text{ e.u.} & [\text{This work}] \\ &= 134.4 \text{ e.u.} & [4] \\ &= 132.746 \pm 0.26 \text{ e.u.} & [7] \end{aligned}$$

Data sources:

$$\begin{aligned} &(1902), \text{ mean } 0-50^{\circ}\text{C} & [1] \\ &(1934), 93-291^{\circ}\text{K} & [4] \\ &(1953), 12-303^{\circ}\text{K} & [7] \end{aligned}$$

n-pentadecane, C<sub>15</sub>H<sub>32</sub>

$$\begin{aligned} S_{298}^{\circ} &= 140.38 \pm 0.30 \text{ e.u.} & [\text{This work}] \\ &= 140.416 \pm 0.28 \text{ e.u.} & [7] \end{aligned}$$

Data sources:

$$\begin{aligned} &(1902), \text{ mean } 0-50^{\circ}\text{C} & [1] \\ &(1953), 12-313^{\circ}\text{K} & [7] \end{aligned}$$

n-hexadecane, C<sub>16</sub>H<sub>34</sub>

$$\begin{aligned} S_{298}^{\circ} &= 148.07 \pm 0.40 \text{ e.u.} & [\text{This work}] \\ &= 149.8 \text{ e.u.} & [6] \\ &= 148.09 \pm 0.29 \text{ e.u.} & [7] \end{aligned}$$

Data sources:

$$\begin{aligned} &(1902), \text{ mean } 0-50^{\circ}\text{C} & [1] \\ &(1949), 80-300^{\circ}\text{K} & [6] \\ &(1953), 12-320^{\circ}\text{K} & [7] \end{aligned}$$

tetraphosphorus decasulfide, P<sub>4</sub>S<sub>10</sub>

$$\begin{aligned} S_{298}^{\circ} &= 91.29 \pm 0.20 \text{ e.u.} & [\text{This work}] \\ &= 91.24 \text{ e.u.} & [8] \end{aligned}$$

Data source:

$$(1965), 6-345^{\circ}\text{K} \quad [8]$$

### References to Heat-Capacity Data

- [1] Mabery, C. F. and Goldstein, A. H., On the Specific Heat of Vaporization of the Paraffin and Methylene Hydrocarbons, *Am. Chem. Jour.* 28, 66-78 (1902).
- [2] Parks, G. S., Huffman, H. M., and Thomas, S. B., Thermal Data on Organic Compounds. VI. The Heat Capacities, Entropies and Free Energies of Some Saturated, Non-Benzenoid Hydrocarbons, *J. Am. Chem. Soc.* 52, 1032-1041 (1930).
- [3] Huffman, H. M., Parks, G. S., and Barmore, M., Thermal Data on Organic Compounds. X. Further Studies on the Heat Capacities, Entropies and Free Energies of Hydrocarbons, *J. Am. Chem. Soc.* 53, 3876-3888 (1931).
- [4] Parks, G. S. and Light, D. W., Thermal Data on Organic Compounds. XIII. The Heat Capacities and Entropies of n-Tetradecane and the Hydroxybenzoic Acids. The Relative Free Energies of Some Benzenoid Position Isomers, *J. Am. Chem. Soc.* 56, 1511-1513 (1934).
- [5] Osborne, N. S., and Ginnings, D. C., Measurements of Heat of Vaporization and Heat Capacity of a Number of Hydrocarbons, *J. Res. Natl. Bur. Std.* 39, 453-477 (1947).
- [6] Parks, G. S., Moore, G. E., Renquist, M. L., Naylor, B. F., McClaine, L. A., Fujii, P. S., and Hatton, J. A., Thermal Data on Organic Compounds. XXV. Some Heat Capacity, Entropy and Free Energy Data for Nine Hydrocarbons of High Molecular Weight, *J. Am. Chem. Soc.* 71, 3386-3389 (1949).
- [7] Finke, H. L., Gross, M. E., Waddington, G., and Huffman, H. M., Low Temperature Thermal Data for the Nine Normal Paraffin Hydrocarbons from Octane to Hexadecane, *J. Am. Chem. Soc.* 76, 333-341 (1954).
- [8] Clever, H. L., Westrum, Jr., E. F., and Cordes, A. W., Heat Capacities and Thermodynamic Properties of Globular Molecules. XIV. Tetraphosphorus Trisulfide, Tetraphosphorus Triselenide, and Tetraphosphorus Decasulfide between 5 and 350 degrees K, *J. Phys. Chem.* 69, 1214-1219 (1965).

## 2. Vapor Pressures

The vapor-pressure, heat of vaporization, and ortho-baric density data are being accumulated on the aliphatic hydrocarbons, alcohols, carboxylic acids, condensed polyaromatics, organo-nitrogen compounds, and others. The heat of vaporization and the ortho-baric densities will be used to help formulate the vapor-pressure equations for the various substances through the Clapeyron relation wherever possible.

## 3. Developments in Computer Calculations

In anticipation of the conversion of the computer at the National Bureau of Standards from the IBM 709<sup>4</sup> to UNIVAC 1108, some effort was spent in becoming acquainted with the new computer. Further efforts will be needed before the existing computer codes can be converted for use with the UNIVAC 1108. Codes for analyzing vapor-pressure data are being developed.



## Section II

### A Non-Biologist Views Thermodynamic Problems in the Biological Sciences

George T. Armstrong  
Heat Division, Institute for Basic Standards

Text of a lecture given before the Heat Division Colloquium  
at the National Bureau of Standards, February 1967.

#### 1. Introduction

About two years ago representatives of NASA approached us with a request for a review of thermodynamic properties of substances that would be of importance in the possible spontaneous origin of life, which is of interest to them in their exobiology program. The circumstances under which life could conceivably arise in the other planets was their particular concern. Without going into the likelihood of their being able to obtain a satisfactory answer to their main problem, we were glad to undertake a narrow technical problem, which was to gather information currently available that would permit thermodynamic studies of the processes other workers might postulate.

In this work we did not rely upon our own judgment for the selection of compounds, but relied upon the advice of Professor Harold Morowitz of the Department of Biophysics and Molecular Biology at Yale University. The general group of compounds which we undertook a review of was the compounds of the elements CHNOPS, containing one carbon atom or less per molecule. However, though numbering several hundred, this was obviously an inadequate set of compounds for the purpose. The thought of opening up the whole field of organic compounds appalled us.

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Princeton, New Jersey

The dilemma was resolved for us by Professor Morowitz with his concept of "Ubiquitous Compounds". The ubiquitous compounds, in a nutshell, are those compounds which available evidence indicates are present in every living thing. Their existence, by inference, is required with a reasonable degree of probability for the formation of life of the variety that we know. Of course we draw a complete blank if we try to conceive of forms of life essentially dissimilar chemically to that found on earth, as we do not really know chemical limitations on life.

The examination of the literature on these compounds was a revelation to us of a vista into the thermodynamic processes of living things, and into molecular biology and biophysics. The thoughts I am presenting today represent some of the results of scanning these vistas from the point of view of a non-biologist.

It is readily apparent even to the non-specialist in life sciences that there has been, in biophysics and biochemistry, a dramatic emergence of the interpretation of processes occurring in living systems in terms of molecular configurations and interactions. It is now commonplace to find the processes that occur immediately subject to the scrutiny of the detailed molecular configurations and interaction energies in attempts to discern the factors involved that determine such matters as precisely what processes occur, what factors control the specificity of the process that occurs, and what effects changes in the substances or their environment have on the precise process that occurs.

In the understanding of the molecular processes of living systems, next in importance to an understanding of the structural relationships we may place an understanding of the energy relationships among them. In this understanding, thermodynamics has a great deal to offer

## 2. A point of view with regard to study of the thermodynamics of biological substances.

In scanning the thermodynamics of biological systems, recognizing the broad scope of the field, we have attempted to maintain an attitude, not of detachment, but contrariwise, a questioning attitude — Is there any relevance of the subjects we are examining to the work of the National Bureau of Standards, and in particular is it pertinent to the work of the Heat Measurements Section? It is not easy to be wholly objective in this respect. However, we have formulated for ourselves certain guidelines as minimum criteria. To be really relevant to the Heat Measurements Section a subject must:

(a) Be an experimental problem of measurement such that a special calorimetric technique of widespread applicability is needed to handle it satisfactorily, or

(b) Must deal with well defined systems, in the sense of purity and reproducibility, which are either (i) systems of almost universal substance, or (ii) systems of such constitution that they exemplify some fundamental, widespread phenomenon.

We will maintain that among the ubiquitous compounds, previously mentioned, are to be found substances in the category (b). In the next section we shall take some examples from among the ubiquitous compounds, to indicate the nature of their ubiquity, and to indicate some particular thermodynamic problems concerning them which seem to be important currently and for the long range.

The approach, which we suggest by the study of ubiquitous compounds, is similar to one, and can be easily coupled to it in such a way as to complement it, referred to in molecular biology as the use of model compounds, of known structure. Currently the molecular interpretation of short range properties of macromolecules depends almost solely upon the study of model systems.<sup>1</sup>

### 3. Model Compounds (Ubiquitous Compounds)

A number of figures follow which give some view of the kinds of compounds which form the ubiquitous list, and a brief clue to their relationships to the life processes.

The metabolic and other life processes (Figure 1)<sup>2</sup> are characterized by economy of agents and by cyclic process. By economy of agents we refer to the fact that some relatively few substances are found over and over again in various processes. For example, amino acids, fatty acids, and sugars, all are metabolized by processes involving many identical steps. Cyclic processes are processes in which some agents necessary for continuing the process are generated in the course of it. A typical cyclic process is the Krebs Tricarboxylic acid cycle, which is illustrated in Figure 2, for the oxidative degradation of glucose. The structural formulas of the acids occurring at stages of this cycle are shown in Figure 3. These are some of the ubiquitous compounds. The numerous other cycles found in the various biological processes also are sources of "ubiquitous compounds", some being duplicated in many cycles.

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<sup>1</sup> W. Kauzmann, "Factors in Interpretation of Protein Denaturation". *Advances in Protein Chemistry* 14, 1 (1959).

<sup>2</sup> See footnote page 6.

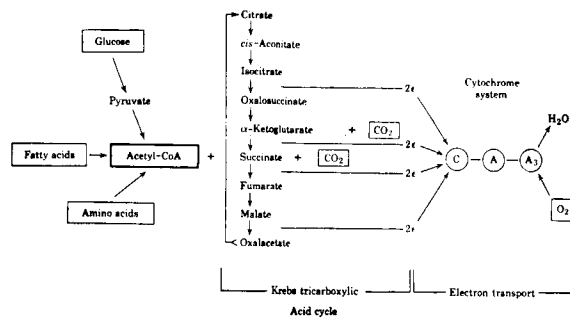


Figure 1. Mutual relationship of the metabolism of various nutritive materials.

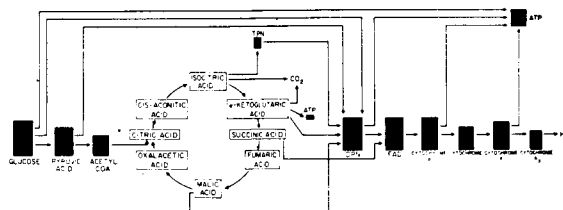


Figure 2. Schematic version of the oxidative metabolism of glucose (1). The solid blocks indicate the relative free energy remaining at each stage.

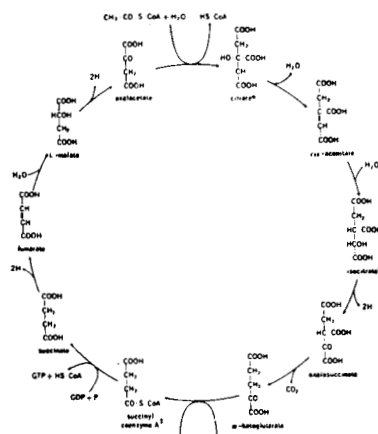


Figure 3. Conversions of the TCA cycle.



Figure 4. Primary structure of human heart cytochrome c (27). The residues given in italics are those found in the corresponding positions in horse heart cytochrome c.

It is a well known fact that the proteins are constituted of  $\alpha$ -amino acids. Perhaps less well known is that the proteins each individually are molecules of definite configuration. The order and total number of the amino acids is fixed. Figure 4 shows the order for one protein of completely known composition. This is the primary structure. The amino acids are linked in the protein by the peptide linkage from which the amino acids may be obtained by hydrolysis. The peptide linkage is diagrammed in Figure 5.

One characteristic of the amino acids is the optical activity, present in all but glycine. Also the many opportunities for hydrogen bonding should be noted.

The primary structure of proteins is further defined by disulfide bridges linking sulfur containing amino acids, as shown in Figure 6.

The secondary structure is the configuration of the polypeptide chain that results from the satisfaction of hydrogen bonding between the peptide N-H and C=O groups. The  $\alpha$ -helix (Figures 7a, 7b), and the  $\beta$ -sheet structures of Pauling and co-workers (Figures 8a, 8b) are illustrations of possible secondary structures for polypeptides.

A tertiary structure is also possible. This is the pattern according to which the secondary structures are packed together within the native protein. Figures 9a and 9b illustrate very schematically such arrangements. Much less is known generally about this than about the primary and secondary structures. But there exist one or two proteins for which the tertiary structure is completely known.

We should like to emphasize that according to recent thought, neither the length nor the equilibrium arrangement of such a protein chain are random. If the protein is reversibly denatured forming a more or less random chain, it can be renatured and thus reforms into the original pattern.

The naturally occurring  $\alpha$ -amino acids number in the 20's and we consider most of them to be ubiquitous.

Another group of ubiquitous compounds is found in the constituents of the ribonucleic acids (RNA) and the deoxy ribonucleic acids (DNA). A model of a segment of a DNA molecule is shown in Figure 10. The molecule's double helix is clearly evident in Figure 10, which shows in black and white the sugar-phosphate chains that make up the principle chains of the helix, and also shows in grey the connecting links of the purine and pyrimidine bases that tie the helices together.

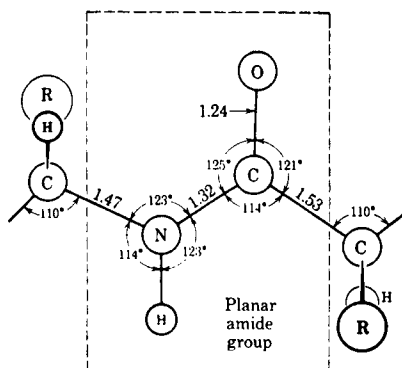


Figure 5. Bond distances and angles of the peptide linkage. Bond distances are in angstroms.

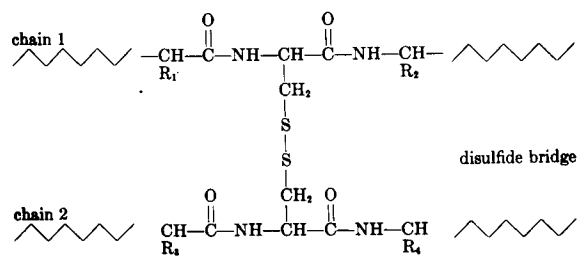


Figure 6. Disulfide Bridge.

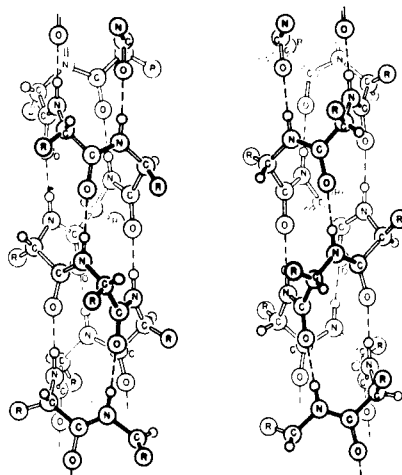


Figure 7a. Left- and right-handed  $\alpha$ -helices.

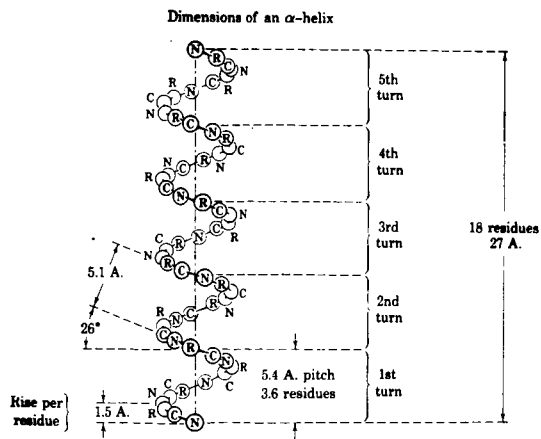


Figure 7b. The  $\alpha$ -helix viewed from another angle, showing dimensions.



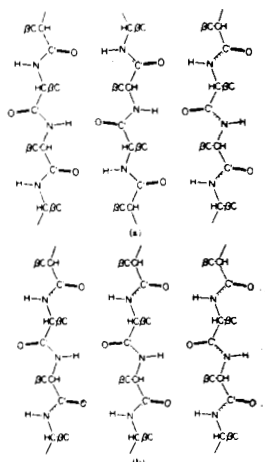


Figure 8a. Parallel (b) and anti-parallel (a) pleated sheet structure. Note positions of inter-chain hydrogen bonds.

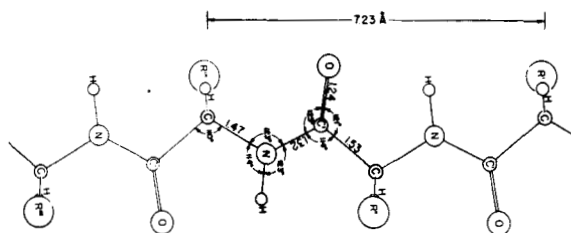


Figure 8b. A completely extended polypeptide chain ( $\beta$ -configuration).

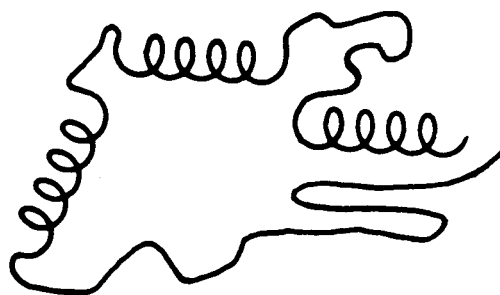


Figure 9a. Schematic configuration of a globular protein with a fractional helical content.

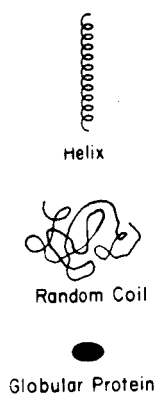


Figure 9b. Schematic representation of several protein configurations. The helix is drawn on a much larger scale than the other two.

The DNA and RNA molecules are among the most important molecules in the world, because the whole genetic basis of the earth's life is incorporated into them and the means for creating the proteins are built into them.

The nearest neighbor configurations of the DNA molecule are shown more schematically in Figure 11. The arrangement of phosphate and deoxy-ribose in the chain is more clearly shown, and the inter-connecting base pairs are indicated, each kind by a characteristic shape. The mechanism for replication is suggested.

Figure 11 shows a hypothetical lock and key type arrangement which makes plausible a geometric determination of the sequence of replication. In a rough calculation (which we cannot vouch for because we have not verified it with a biophysicist) we estimate that the chains zipper up at a rate (rate of introduction of nucleotides) of 1000 to 3000 per second. So, when reproducing itself a DNA molecule is really buzzing along.

It has been possible to demonstrate the reversible character of the denaturation of DNA. The schematic view of the reversible denaturation of DNA is shown in Figure 12. Thus the growing conviction we have of the geometric reproducibility of these large molecules is made plausible by the actual realizability of the re-association of the double helixes.

The constituents of the deoxyribonucleic acids and the ribonucleic acids are remarkably few in number. In Figure 13 is shown one of the most complex units of the chain — the nucleotide. It consists of a phosphate (mono, di, or tri phosphate), a sugar (ribose or deoxyribose), and a base, condensed chemically into a single molecule.

Figure 14 shows the three 5' adenine nucleotides which differ only in mono-, di-, and tri-phosphates, respectively.

Figure 15 shows a more appropriate stereochemical configuration.

The five free bases which make up the linkages between helices are shown in Figure 16. Note that these molecules are very interesting from the point of view of resonances, tautomeric forms, basic characteristics, and potentialities for forming hydrogen bonds.

Figure 17 shows the structure of adenine more in detail.

Figure 18 shows the inter-molecular hydrogen bonding of the base pairs, Adenine-Thymine and Cytosine-Guanine.

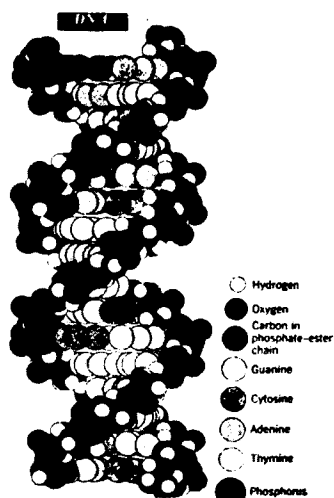


Figure 10. Molecular model of the B form of DNA.

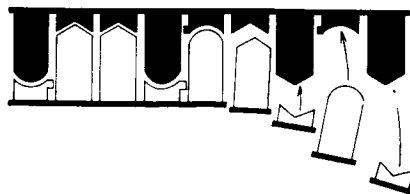
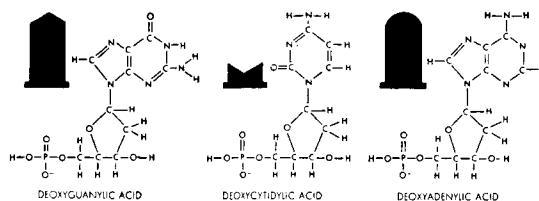


Figure 11. A schematic view of the interlocking configurations of the constituents of the DNA strands, with an indication of a replicating mechanism.

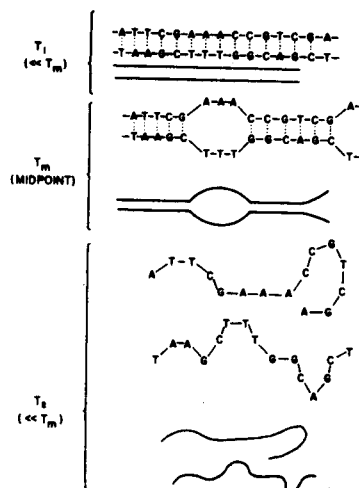


Figure 12. Schematic model for thermal denaturation of DNA

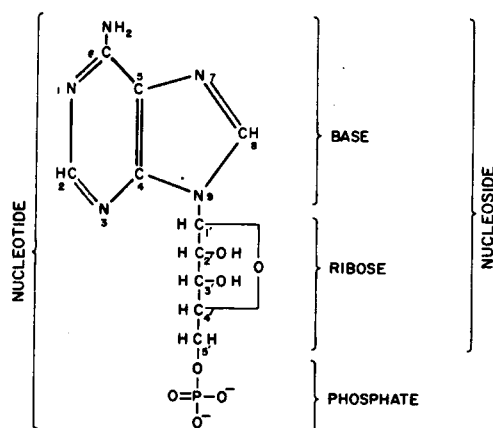


Figure 13. The ribonucleotide adenosine-5'-phosphate (5'-AMP).

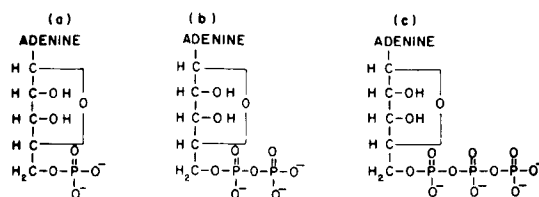
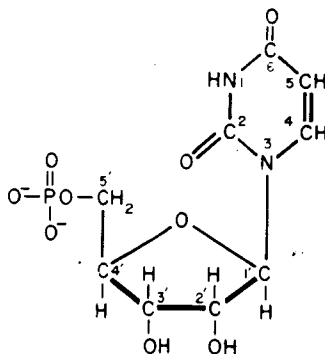


Figure 14. The 5'-adenine nucleotides. Part (a) represents the adenosine-5'-phosphate (5'-AMP); (b) the adenosine-5'-diphosphate (5'-ADP); and (c) the adenosine-5'-triphosphate (5'-ATP).



15. Stereochemical formula for uridine-5'-phosphate, showing the configuration about the carbon atoms of the ribose.

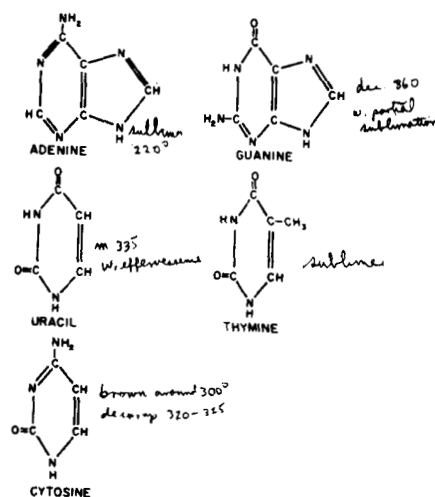


Figure 16. Structures of the free bases.

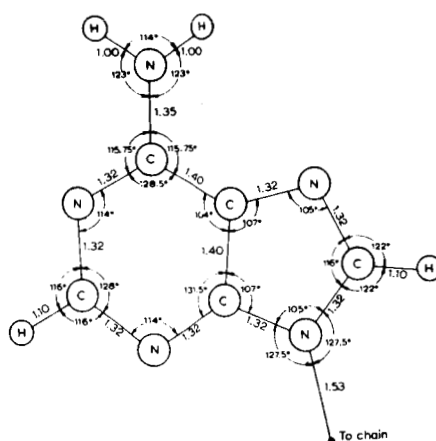


Figure 17. Structure and dimensions of adenine.

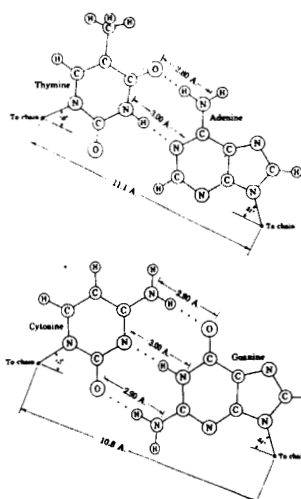


Figure 18. The hydrogen-bonded base pairs of DNA.



The nature of the ubiquitous compounds should now be clear. For instance, the whole molecule shown in Figure 13 and also sub-units of various sizes are ubiquitous. It is fairly obvious that there is no clear dividing line circumscribing the ubiquitous compounds. The list is more or less open ended but rather severely limited. The number of such compounds is in the order of 200. A tentative list is available.<sup>3</sup>

#### 4. Experimental Thermodynamics

Ultimately, for full interpretation of the interactions that occur in the aqueous phases in which these substances are active, one would hope to have a full set of structural and thermodynamic information on the important species present. This is a monumental job. It would require an Institute in itself and many thermodynamicists working for years.

From the most fundamental point of view, it would be desirable to have spectroscopic and thermodynamic data on the gas phases, the crystalline phases, and the aqueous phases of these ubiquitous compounds. This reservoir of data could then be drawn upon by interested biophysicists and biochemists to apply to particular biological processes for interpretation or prediction of the process. Because of the "ubiquitous" nature of the compounds, these data would have greater range of application than any which can be proposed. Except in spotty instances these data are largely lacking.

A limited amount of work along this line is now going on. The work of Stanley Gill at the University of Colorado, Randolph Wilhoit at the Texas A&M University, Hutchens and Stout at the University of Chicago, and undoubtedly others, involves solution calorimetry, combustion calorimetry, or specific heat measurements on selected compounds found among the group.

A far larger group, with which we are less familiar, but including Benzinger at the Naval Medical Center, Philip Ross, Edwin Becker and Robert Berger at NIH, Sturtevant at Yale (La Jolla), Lumry of the University of Minnesota, Biltonen of Johns Hopkins, and others, are working specifically on the thermodynamic problems of interpreting processes occurring in solution. The latter group deal much more with complex systems for which a major problem is the interpretation of the data.

I shall not attempt to review all classes of more limited problems but shall mention a few specifically which have come specially to my attention

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<sup>3</sup> NBS Report 8641, pp. 28-33, February 1965.

## A. Vaporization

Let us return to Figure 10. Note in this figure how large fractions of the molecule participate in internal interactions not involving the solvent, water. Large numbers of the interactions that occur are more similar to interactions in crystalline solids than to interactions of aqueous solutions. If we wish to study the interactions, either hydrogen bonded or between near but not bonded neighbors, we will obtain useful information from vaporization studies of the constituent fragments.

Figure 16 shows some vaporization information available on the free bases in pencilled notes; that is essentially nothing. The occurrence of sublimation of thymine is a clue that vaporization data could be obtained on all of them. Similar information on the amino acids has borne this out. We would expect these substances to sublime reversibly at pressures of the order of magnitude of a micron. We would expect that useful information could be obtained from the existence or absence of dimer formation in the vapor phase, and from the vaporization behavior of selected mixed crystals of the base pairs.

Aside from the energies of vaporization thus obtainable, the existence of a gas phase would lend itself to spectroscopic study. Though the molecules are very complex, the time is probably ripe for study of them. Similar considerations apply to the polypeptides. Some vapor pressure study has already been carried out on the amino acids, though its interpretation is open to question.

## B. Tacticity

Noting the fact that the  $\alpha$ -amino acids are all L-configuration when found naturally, we realize that the chains that they form have an unusual character of optical activity. We believe it is true that the helical character (Figure 7b) of the  $\alpha$ -structure depends upon the identity of the L-configuration in all amino acids. While not directly related to protein structure, the competence has recently been developed to build polymeric substances of isotactic configuration. Such polymers are much more crystalline than non-isotactic polymers. The opportunity now exists to study crystallinity effects in polymers (by means of specific heat studies for instance) that would have been impossible a few years ago.

## C. Problems associated with denaturation of protein

The forces holding native protein in its configuration (See Figure 9b) are of three general types.

- (a) hydrogen bonding
- (b) hydrophobic bonding
- (c) salt linkages

The factors involved in denaturation were reviewed by Kauzmann (1959).<sup>1</sup> Denaturation involves destruction of the secondary and tertiary structure of a protein, but no disturbance of the primary structure. However, theories of the process are not uniformly accepted.

One picture of the denaturation process calls for removal of non-polar (R) groups from the interior of the molecule, where they are out of contact with water, to an exterior position, where they interact with the water. The effect of this is thermally small, but a large decrease of entropy causes an endergonic Gibbs energy change,  $\Delta F = +3000$  to  $+5000$  cal mol<sup>-1</sup>, and a large change in specific heat.

A picture has been proposed (Frank and Evans)<sup>4</sup> of the formation of "icebergs" (regularly hydrogen-bonded water), in the vicinity of the non-polar group. There would be a large decrease of entropy as a result of the formation of these crystals.

Some insight into the possible nature of these icebergs can be gained from a study of the crystalline hydrates that form at elevated pressures between water and methane, ethane or propane. These crystals are examples of clathrate or inclusion compounds. A study of the heat capacities of these would be appropriate. It is interesting to note the close relationship between the study of protein denaturation and the understanding of the structure of water, whose study has had a renaissance.

The use of model compounds does not seem to offer completely unambiguous interpretations of the processes occurring in denaturation. The actual denaturation process itself must also be studied calorimetrically. This kind of study has been done by Sturtevant, but is quite difficult. There is an opportunity here for the development of experimental heat measurement techniques which will allow greater refinement of these measurements.

The direct measurement of  $\Delta C_p$  for the reaction is considered to be valuable from the point of view of understanding the hydrated states before and after. While by no means an optimum method, the achievement of the  $\Delta C_p$  measurement has recently been accomplished by Wadso using an ordinary reaction calorimeter. He calibrates electrically before and after the reaction, and the difference in the energy equivalent is  $\Delta C_p$  for the reaction. Here he is working at a level where the differences he is looking for are about 0.1% of the total heat capacity. A new instrumental technique would be highly desirable.

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<sup>4</sup> H.S. Frank and M.W. Evans, J. Chem. Phys. 13, 507 (1945).

A final problem is of some interest: The free energy changes in solution in biological systems are often carried out in highly buffered solutions of controlled ionic strength, because this is the only condition under which some important species are active. The substances are thus definitely not in their thermodynamic standard states. An analysis of the differences in activity or free energy of the practical solutions from the thermodynamic standard state is highly desirable to place the many hydrolysis and other measurements that have been made onto the same basis as the rest of thermodynamics.

In conclusion, in the thermodynamics of biologically active materials we find not so much an infinite reservoir of problems, but a reasonably outlineable basic problem of definable extent involving substances of extremely wide applicability. The elucidation of these substances would at least provide the basis for biologically oriented studies to be continued and elaborated on a basis comparable to that which has been applied throughout traditional theoretical and practical chemistry.